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Original article

# DISTRIBUTIONAL CONSIDERATIONS IN ECONOMIC RESPONSES TO ANTIMICROBIAL RESISTANCE

*Running title: Distribution, economics and AMR*

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**SUMMARY:** Antimicrobial resistance is a major and increasing problem globally. Economics has engaged with this issue increasingly over the last 20 years. Much of this concerns assessments of the cost of various forms of resistance, but it also includes economic analyses of interventions and policies designed to contain resistance. Analysis has, however, thus far largely neglected possible distributional issues associated with such interventions and analysis. The paper explores three normative bases for the conduct of economic analysis: welfarism; extra-welfarism focused on health gain; and extra-welfarism focused on capability assessment. It then considers issues intrinsic to antimicrobial resistance in terms of the distributional implications and how these might be handled within economic analyses from each of the normative perspectives, before considering the actual focus of empirical studies on these distributional issues. The paper concludes that the different normative starting points for economic analysis will affect how distributional issues are incorporated into analysis, but suggests that all analyses could benefit from greater discussion of these issues.

**KEYWORDS:** Antimicrobial resistance; economic evaluation; distributional issues; free-riding; time preference.

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# SUMMARY

Antimicrobial resistance is a major and increasing problem globally. Economics has engaged with this issue increasingly over the last 20 years. Much of this concerns assessments of the cost of various forms of resistance, but it also includes economic analyses of interventions and policies designed to contain resistance. Analysis has, however, thus far largely neglected possible distributional issues associated with such interventions and analysis. The paper explores three normative bases for the conduct of economic analysis: welfarism; extra-welfarism focused on health gain; and extra-welfarism focused on capability assessment. It then considers issues intrinsic to antimicrobial resistance in terms of the distributional implications and how these might be handled within economic analyses from each of the normative perspectives, before considering the actual focus of empirical studies on these distributional issues. The paper concludes that the different normative starting points for economic analysis will affect how distributional issues are incorporated into analysis, but suggests that all analyses could benefit from greater discussion of these issues.

**KEYWORDS:** Antimicrobial resistance; economic evaluation; distributional issues; welfarism; extra-welfarism; health gain; capability approach.

# INTRODUCTION

After a brief hiatus, antimicrobial resistance has again become a major focus of policy makers both in the UK (Davies, 2013) and internationally (World Health Organisation, 2012). There is increasing concern that the future of infectious disease treatment will look very different to that enjoyed in the last 70 years, with many of the advances in medical treatment that have taken place over this time now being threatened by the potential inability to control infection (Smith & Coast, 2013; Davies, 2013; World Health Organisation, 2012; Cooper, 2013) and potentially huge economic costs (Taylor, Hafner, Yerushalmi, Smith, Ballasio, Vardavas et al. 2014; O'Neill, 2014). Whilst there have been successes in reducing some resistant infections, such as MRSA and *C. Difficile*, others, including *E.Coli* and *Klebsiella*, are on the rise (Davies, 2013). In the UK, there has been a policy step-change with the publication of the recent Chief Medical Officer's (CMO) report, which includes recommendations around both "preserving the effectiveness of our existing antimicrobial agents" and encouraging "the development of new agents in the future" ((Davies, 2013), p. 19), although there is little in the way of specifics, beyond encouraging 'stewardship' programmes and encouraging the alignment of incentives between pharmaceutical companies and the societal need for new antibiotics. Recommended actions are not limited to the UK but also to an increased lobbying by the UK on this issue within the international community, and there has subsequently been a large investment in research funding for antimicrobial resistance through the National Institute for Health Research (NIHR), Research Councils UK (RCUK) and the Wellcome Trust.

The recent UK CMO report sees the potential economic contribution almost entirely in terms of the market failures associated with the differing incentives of the pharmaceutical industry and broader society (Davies, 2013). The same is true of other writings in this area (Buckland Merrett, 2013; World Health Organisation, 2012) but although this is an important issue, it is just one among a number of areas where economic analysis might make a contribution to the challenge of antimicrobial resistance. First, economic analysis can be used in studying some of the fundamental challenges associated with antimicrobial resistance, all of which have important distributional issues. These fundamental challenges relate to three areas of conceptual understanding. The first of these is free-riding associated

with the nature of antibiotic resistance. Within economics, antimicrobial resistance can be conceptualised as a negative externality associated with the consumption of antimicrobials (Coast, Smith & Millar, 1998). Externalities occur when an economic agent (here, the patient/consumer), makes the decision to take an action (here consume an antimicrobial) taking account of only the costs and benefits to themselves, and not those incurred by others in society, and thereby acting in a manner that results in a higher level of consumption than is socially optimal. These externality decisions are being taken constantly across the world by different combinations of consumers and providers. The second fundamental challenge concerns time preference, and the relative costs and benefits of consumption now versus future consumption. And the third challenge concerns the global nature of resistance.

Second, economics also provides analytical and empirical contributions in terms of :

1. increasing the understanding of the impact of resistance through a focus on costs, including direct health costs (see, for example, amongst a large number of similar studies (Carmeli, Troillet, Karchmer & Samore, 1999; Cosgrove, 2006; Cosgrove, Kaye, Eliopoulous & Carmeli, 2002; Parvizi, Pawasarat, Azzam, Joshi, Hansen & Bozic, 2010; Alam, Cohen, Butler, Dunstan, Roberts, Hillier et al. 2009)), costs to whole health systems (Smith & Coast, 2013) and costs to whole economies (Smith, Yago, Millar & Coast, 2005; Taylor et al., 2014);
2. generating better understanding of the efficiency of interventions that utilise antimicrobials (Coast, Smith & Millar, 1996) across the whole spectrum of healthcare provision;
3. developing policy to contain resistance both in the context of individual nations (Coast et al., 1998; Smith & Coast, 1998; Laxminarayan & Brown, 2001) and internationally (Anomaly, 2010) including policy around generating new antimicrobials (World Health Organisation, 2012; Outtersen, 2014);
4. evaluating policies, such as stewardship policies or diagnostic tools, that aim to reduce use both at national (Smith, Yago, Millar & Coast, 2006; Wilton, Smith, Coast, Millar & Karcher, 2001; Oppong, Jit, Smith, Butler, Melbye, Molstad et al. 2013; Laxminarayan, Parry, Smith & Klein, 2010) and international levels (Smith & Coast, 2001; Smith & Coast, 2002).

There are also a number of aspects of antimicrobial resistance that it is helpful to understand before continuing. The first is that it is an extremely complex topic biologically, where there are multiple micro-organisms and anti-microbials that might be examined (World Health Organisation, 2012). In some ways, it is helpful to consider the issue as a class of problem, rather than a single problem. The second is that the information available is imperfect. There is a lack of knowledge about basic epidemiology (although this varies by both region and pathogen), causal pathways, likely impacts from policies that result in diffuse effects, and the likelihood of identifying new antimicrobials. All of this results in extreme uncertainty not just about how to deal with the problem, but about the size of the problem itself and the likely size in the future under different possible 'futures'. The problems have a direct parallel with those of climate change or global warming (Broome, 1992). The third also parallels the climate change argument, in that current actions have such a small individual cost that providing incentives not to consume may be very challenging, thus potentially requiring a more regulatory or coercive approach. The fourth is that eradication of resistance is not an appropriate goal, but that instead the aim is to contain, manage and live with resistance (World Health Organisation, 2001), optimising the use of antimicrobials across time (Smith & Coast, 2002).

The paper turns now to exploring the nature of the normative economics that might be used in analyses of antimicrobial resistance and related issues, focusing on three distinct viewpoints about what is important in the evaluation of health and related interventions. The paper then continues by investigating issues with distributional implications that are intrinsic to the analysis of antimicrobial resistance, and their handling from different normative viewpoints. Third, the paper considers the reporting of distributional impacts in a small number of empirical examples of economic assessments of policies and interventions in the area of antimicrobial resistance. Finally, some general conclusions are drawn.

# **MORAL VIEWPOINTS AND NORMATIVE ECONOMIC ANALYSIS**

Normative economic analysis focuses not on trying to describe or explain economic issues but on exploring what actions should be taken if particular ends are to be achieved. In general, economists start from the position that resources are scarce and that their use for one purpose incurs an opportunity cost (the lost benefit of using them for the next best thing). Given that there are choices about how resources are used, economists are interested in whether they are used in the ‘best’ way possible, where the ‘best’ way possible is concerned with getting the maximum from these resources. That is, whether resources are used ‘efficiently’. Ideas of efficiency are inextricably linked with such notions of maximisation, but such ideas can be interpreted in different ways by different groups of economists. This paper will consider three such interpretations. These interpretations provide the three main approach to economic analysis currently used by economists in the area of health. They differ first and foremost in relation to their ‘evaluative space’ – that is, what they consider important to evaluate (Sen, 1993). There are also, however, quite different implications within the three approaches in how distributional issues might, and should, be considered.

## **Interpretation 1: traditional utility maximisation within welfarism**

Traditionally within economics, the concern has been with ‘utility’ maximisation: referred to here as the ‘welfarist’ approach. (It should be noted that the terminology of ‘welfarist’ here refers only to this dominant model within economic theory; it does not relate to other, pluralist, accounts of welfare (Arneson, 2000).) Utility is a subjective concept which has been interpreted differently across history (Blaug, 1996; Cooter & Rappoport, 1984; Hargreaves Heap, Hollis, Lyons, Sugden & Weale, 1992; Roncaglia, 2005), but which is related to satisfying desire (Cooter & Rappoport, 1984) through the consumption of goods, services and leisure time (Culyer, 1989). Health services are one such good that can be consumed to produce utility, although typically indirectly through enabling more consumption of direct-utility providing goods and services. It is also generally assumed that inter-

personal comparison of utility is not possible (Reinhardt, 1998). The focus is also usually on 'expected' utility, that is, the evaluation of the utility that would be expected, *ex ante*, from a particular course of action. Within the welfarist approach a number of assumptions are made. It is assumed that: individuals are the best judges of their own utility; an improvement in an individual's utility without a loss in any other individual's utility is an improvement in total utility; and (because these two criteria alone would result in almost entire policy paralysis, given that almost no decisions result in no losers) that if individuals gaining from a policy change could hypothetically compensate those losing from the change, that would also provide an improvement in total welfare (Hicks, 1941; Kaldor, 1939). This approach means that economists can abstract themselves from distributional considerations, with their focus being on 'economic' decisions that lead to utility maximisation rather than political decisions about redistribution of actual gains and losses (Blaug, 1996).<sup>1</sup>

This approach is operationalised in evaluation through cost benefit analysis (Mishan, 1988), where costs and benefits from all perspectives within society are included, usually with the valuation of benefits in monetary terms. This monetary valuation brings its own distributional considerations (arising from the use of willingness to pay methods that rely on ability to pay and thus may favour treatment of those conditions that affect better-off individuals), although there are approaches to avoiding these (for example, concentrating on proportions of income rather than absolute amounts) (Donaldson, Birch & Gafni, 2002). The welfarist approach provides the first moral viewpoint for economic analysis: one in which the concern is for maximising expected utility (societal welfare), with a clear theoretical separation between economic considerations of such maximisation and distribution of societal welfare between members of that society.

## **Interpretation 2: health maximisation within the standard extra-welfarism of health economists**

Within health economics, particularly within the last 20 years, this general approach outlined above of efficiency and maximisation has been interpreted specifically in relation to health (Culyer, 1997). In this paradigm, health can be produced through the allocation of resources, and it is valued in its own



right and not just because it produces utility (Coast, 2009). Health gains are valued *ex post* using indices of health status and generally transformed into Quality Adjusted Life Years (QALYs) or an equivalent form of measure (Williams, 1985). Although, theoretically, extra-welfarism can accommodate a broader interpretation of non-utility information than ‘just’ health (Brouwer, Culyer, van Exel & Rutten, 2008), in practice, this has been its interpretation. The basis for this exclusive focus on health maximisation in this paradigm is less clear and seems to be largely related to early papers that either used this option without discussion (Fanshel & Bush, 1970; Weinstein & Stason, 1977) or justified pragmatically as the objective most likely to gain agreement (Culyer, 1988). In relation to the choice of maximisation as a decision rule, however, it does not appear that appeal can be made to the same arguments that are used within welfarism, as health is both produced and allocated simultaneously, and it cannot be redistributed, meaning that (hypothetical) compensation is not possible (Coast, 2009). Rather, it seems that health economists working within this approach are happy to compare health across persons (Brouwer et al., 2008; Williams, 1996) and that the theoretical distinction between efficiency and distribution is no longer upheld (Coast, 2009). Under this paradigm, therefore, economists are “endorsing the ethical position that the total sum of health produced within the health care system is what matters, no matter how that health is distributed” ((Coast, 2009), p.789). There are various implications of this such as, *ceteris paribus*, the young will be preferred to the old (Harris, 1987), but it is a view that is generally upheld, despite some health economists seeking evidence from the public that would enable them to adjust QALYs for equity concerns (Dolan, Shaw, Tsuchiya & Williams, 2005; Tsuchiya, Dolan & Shaw, 2003; Tsuchiya & Dolan, 2009; Donaldson, Baker, Mason, Jones-Lee, Lancsar, Wildman et al. 2011). It should be noted that, because of the focus on health maximisation, the cost side of such analyses is usually also restricted to a health service perspective.

This approach is operationalised in evaluation through cost-effectiveness analysis with the QALY as the unit of outcome (sometimes referred to as cost-utility analysis). The extra-welfarist health gain approach provides the second moral viewpoint for economic analysis: one in which the concern is for maximising achieved health and there is no theoretical separation between economic and distributional considerations so that the associated distribution is, by default, that achieved through maximisation.

### **Interpretation 3: capability assessment within a broader extra-welfarism**

There is increasing interest within health economics (Mooney, 2004; Anand & Dolan, 2005; Coast, Smith & Lorgelly, 2008; Ruger, 2010) in applying the broader extra-welfarism advocated within the capability approach of Amartya Sen (Sen, 1992; Sen, 1993; Robeyns, 2005; Robeyns, 2006; Alkire & Deneulin, 2009) to economic assessments. The capability approach focuses on functionings and capabilities, where functionings are the things that a person ‘manages to do or be in leading a life’ (Sen, 1993, p.31) and capabilities are ‘the alternative combinations of functionings the person can achieve, and from which he or she can choose one collection’ (Sen, 1993, p.31). These functionings and capabilities become the focus of analysis in evaluations conducted through the capability approach.

The capability approach more generally has gained support within health (Entwistle & Watt, 2013; Law & Widdows, 2007; Ariana & Naveed, 2009; Venkatapuram, 2011) and has even been applied to the analysis of healthcare associated infection (Millar, 2013). Within health economics, recent work has advocated the use of a capability approach (Coast et al., 2008; Anand & Dolan, 2005; Lorgelly, Lawson, Fenwick & Briggs, 2010) and a number of research groups are conducting work to generate measures that can be used in assessing capability within economic analysis (Simon, Anand, Gray, Rugkasa, Yeeles & Burns, 2013; Lorgelly, Lorimer, Fenwick & Briggs, 2008; Al-Janabi, Flynn & Coast, 2012; Flynn, Huynh, Peters, Al-Janabi, Clemens, Moody et al. 2015). One example of such a measure is ICECAP-A where participatory approaches were used to generate a descriptive system for a measure that can be used for assessing capability within an economic assessment, with dimensions including capabilities for autonomy, achievement, stability, enjoyment and attachment (Al-Janabi et al., 2012; Flynn et al., 2015). Such approaches are not inextricably linked to maximisation of total capability, and economists have started to explore the possibility of focusing on achieving sufficient capability within the population (Ruger, 2010; Mitchell, Roberts, Barton & Coast, 2013) drawing on approaches taken by the multi-dimensional poverty literature which focus resources only on those with insufficient capability (Alkire & Foster, 2011). Like health, however, it is clear that capabilities

cannot be compensated for within their own evaluative space and that economic and distributional considerations must be dealt with simultaneously (Coast, 2009). As with the welfarist (rather than extra-welfarist) approach, costs from across society would be included in the analysis.

This approach is only just beginning to be operationalised in health economics and there are options for how it is used in evaluation although the most developed currently are to maximise either Years of Full Capability (equivalent) or Years of Sufficient Capability (equivalent) (Mitchell et al., 2013). The assessment of capabilities within a broad extra-welfarist framework provides the third moral viewpoint: one in which the concern is with increasing capability and where choices have to be made about the approach to distribution within the general framework.

These three normative economic interpretations each have different implications for the further consideration of economic and distributive consequences within the context of antimicrobial resistance. The welfarist approach is able to treat these implications as being separable; the standard health economics approach treats the maximisation of health as an appropriate distributional aim; and the capability approach has a broader and more flexible focus in which distribution and economic considerations must also be dealt with simultaneously but within which maximisation may not be considered the appropriate aim. Each of the different approaches also prioritises a different outcome which may, again, have different ethical implications for the economic analysis of antimicrobial resistance.

# **ISSUES INTRINSIC TO ANTIMICROBIAL RESISTANCE, THEIR DISTRIBUTIONAL IMPACT AND THEIR HANDLING WITHIN THE VARIOUS NORMATIVE ECONOMIC APPROACHES**

The paper now turns to the distributional challenges inherent in analytic approaches to antimicrobial resistance. Economic analysis is largely concerned with assessment of costs and benefits as a guide to action, and so distributional issues are concerned with the gainers and losers associated with particular choices; here in relation to antimicrobial resistance (including the choice to do nothing). These are discussed with respect to the three ‘problems’ posed by antimicrobial resistance to aspects of distribution: free-riding; time preference; and the global nature of resistance.

Each of these problems is examined in light of the three normative economic perspectives discussed above.

## **Free-riding and distribution among individuals**

Antimicrobial resistance is, by its very nature, an inter-personal issue. The decisions that individuals make with regard to consumption of antimicrobials impact not just on themselves but on others around them. Those taking antimicrobials are not required to take into account the cost of their action in terms of the build up of resistance within the community and so they are likely to ignore these costs in making their decision to consume. Even very small benefits may therefore outweigh the costs of consuming antimicrobials (which are often not expensive), leading to overconsumption.<sup>2</sup> The person who consumes effectively ‘free-rides’ because they do not take account of all of the costs imposed on society (Coast et al., 1998). The likelihood of people free-riding in relation to this particular decision seems to be particularly high, given that each person, if aware of the issue at all, will be cognisant that their own consumption of antibiotics is ‘a drop in the ocean’ relative to the total consumption of antimicrobials, particularly when thinking across both human and animal consumption (Coast et al.,

1996). The extent of free-riding that is possible is likely to depend on the health care system where the decision is located. Where antimicrobials are available without restriction (for example, available for purchase ‘over-the-counter’ rather than through a gatekeeper such as a general practitioner), the extent of such free-riding may be greater than where a doctor has to decide that an antimicrobial is required. Even where there are restrictions, however, the final decision as to whether to consume will be the product of both the patient’s and the gatekeeper’s views. Overall, the antimicrobial resistance problem is the accumulation of many millions of decisions by different decision makers for different patients in different health systems and facing different personal, financial and organisational incentives. Economic policies (including some of those discussed below) aim to induce consumers to internalise the costs of the externality, but because of the diffusion of the problem in relation to resistance, such policies may be very challenging.

Economists tend to think about these issues in terms of adjusting for market failure (Hodge, 1995; Pearce & Turner, 1990). Methods of adjusting for market failure in the context of antimicrobial resistance might include system interventions or clinical interventions. Examples of system interventions would be taxation (Pigovian taxes / pollution charges) (Coast et al., 1998), subsidy (Laxminarayan et al., 2010), permits (Smith & Coast, 1998) or regulation (Coast et al., 1998). Examples of clinical interventions might be better diagnostics (Kolmos & Little, 1999; Rice, 2011; Oppong et al., 2013), or educational campaigns providing better information (Goossens, Guillemot, Schlemmer, Costers, Van Breda, Baker et al. 2006; Huttner, Goossens, Verheij & Harbarth, 2010), combined with a gatekeeping role from health care providers. Economic assessments or economic evaluations provide the means of determining how well these particular adjustments might alleviate the free-riding problem, by providing information about the relative gains or losses in value associated with these adjustments.

Economic evaluation of such interventions can be thought about from each of the normative economic perspectives outlined above. From a welfarist perspective, the aim is to maximise utility. In the context of antimicrobial consumption such utility may not be related just to health improvements, but might also, for example, incorporate other factors specific to the decision point such as being able to attend a wedding or an important meeting at work, or avoid having to take time off work for a sick

child. Such aspects may be valued highly and may increase the utility associated with consuming antibiotics. In a welfarist world it would be legitimate to take account of such factors in assessing the value of immediate consumption. Other factors that might need to be taken into account would include any distortion to the economy imposed by taxation intended to deal with the problem as well as any possible benefits in terms of option or existence value (the idea that individuals have some personal utility from knowing that the option for them to consume antimicrobials will be retained for them in the future) (Coast, Smith & Millar, 2006). One difficulty is that the utility benefits to the unknown beneficiaries from reduced resistance may be much more difficult to discern (Coast et al., 1996). A second is that the value of these additional factors may differ across groups in society (for example, the highly paid may place greater value on avoiding lost work time and thus on receiving an antimicrobial) and this may affect the ultimate distribution of benefits.

The extra-welfarist health gain perspective would instead focus on the potential losses to health for those not receiving an antimicrobial and potential health gains associated with avoiding greater resistance. Whilst health gains would be treated equally for all there might be distributional effects that would be ignored, for instance, if one group in society were particularly affected by resistance (for example, TB is associated with poverty and those affected by MDR-TB or XDR-TB are most likely to be found in these groups).

A capability approach to this issue would focus on enhancing capability, even if the need for enhanced capability were not recognised by certain groups. There are two ways in which an analysis conducted from a capability approach might differ from the other normative approaches in how it treats distributional issues associated with free riding. The first is that it might start from the position that those with minor, self-limiting conditions are not sufficiently impeded in terms of capability to receive value from antimicrobials such as antibiotics (unlike in either the welfarist/health-based extra-welfarist approach where any utility/health gain would be valued) and so in an evaluation the value given to current antimicrobial consumption for some groups might be zero. The second draws on the dual focus of the capability approach on personal well-being and agency. Agency is the notion that a person may have goals beyond their own personal well-being (Sen, 1993), and if people feel a moral

responsibility to avoid resistance within society there may be an agency value that should be incorporated into an economic assessment in addition to the assessment of personal capability.<sup>3</sup>

The precise implications of these different normative economic approaches in relation to distributional issues arising from the free-riding aspect of resistance is not clear and likely to require empirical analysis. *A priori*, however, there are clear areas of difference in how value would be attributed and thus the likelihood of different distributional implications.

## **Distribution among generations and the time-preference problem**

Antimicrobial resistance is, intrinsically, an inter-generational issue. The externality impacts not just in the immediate timeframe, but (far) into the future. The decisions that are made today, this year, next year, will impact on the likelihood of antibiotic effectiveness in ten, twenty, fifty, one hundred years time. If we see the antimicrobial resource as, essentially, finite<sup>4</sup> there are choices about how to distribute the resource across current and future generations. Economists generally tend to think of these issues in relation to time preference, or expected productivity gains.

The empirical literature on time preference does not offer a strong guide as to how these inter-generational issues should be treated in economic analysis of interventions and policies for antimicrobial resistance. A recent examination across a number of studies found hugely varying mean rates, with some rates being so high that the emphasis on current benefits would be huge (Asenso-Boadi, Peters & Coast, 2007). This work did find, however, that people were more likely to express smaller rates of time preference when asked about longer delays in receiving benefits, and noted that the high empirical time preference rates are not in line with the sorts of normative arguments that are considered when inter-generational equity is discussed.

The issue of time preference has previously been discussed in relation to antimicrobial resistance, with a particular focus on the difference between social discount rates that ‘should reflect collective value judgements and moral issues, rather than just the preference that individuals have for their own consumption over time’ ((Coast et al., 1996), p.221). Indeed, it has been noted that the focus on

averaging empirical time preference rates obtained from current populations as a way of obtaining a societal rate is a relatively new idea (Krahn & Gafni, 1993), and that it may be preferable for policy makers to utilise very low or zero social time preference rates, as even quite low values can relatively quickly mean that the current value of large future values may be extremely small (Coast et al., 1996).

Different choices about discount rates (which numerically reflect time preference) in economic analysis will lead to different distributional impacts. High discount rates would result in an almost exclusive focus on the current population, and would probably also mean that the focus would be on interventions intended to reduce transmission of antimicrobial resistance, which has relatively short term gains, rather than interventions intended to reduce emergence of new resistances, which may be further down the line (but where the total benefits in the absence of discounting may be much greater). (This issue is examined in greater detail elsewhere (Coast, Smith, Wilton, Karcher & Millar, 2002)). In the area of global warming, which shares many features with antimicrobial resistance, there have been arguments for the use of a zero-discount rate on the grounds of the potential harm that would be imposed on future generations by a positive rate and the utilitarian view that all should count equally and thus that there should be impartiality between generations (see (Broome, 1992) for a full exploration of the arguments for and against a zero discount rate in relation to global warming).

These different ideas can be linked to the different normative bases for economic analysis. The welfarist approach generally gives primacy to the use of individual preferences in decision making, suggesting that here the focus might be on using empirical time preference rates. The extra-welfarist perspectives, both health and capability focused, in contrast, may place greater emphasis on policy makers taking a role in defining appropriate societal discount rates for decisions around antimicrobial resistance given the reduced emphasis on use of individual preferences (Brouwer et al., 2008). It is worth noting however that, in practice, many analyses use a standard discount rate determined on a national basis.



## **Distribution among geographical locations and the global problem**

Geographical distribution of costs and benefits in relation to economic assessments may also be important. The nature of antimicrobial resistance is such that it does not respect regional or national boundaries, with resistant organisms being able to travel from one setting to another just as easily as sensitive ones (Coast et al., 1998). Globalisation has increased the rate at which infectious diseases can travel, and resistances identified in one area are rapidly found in other countries and on other continents. Such spread will be dependent on many epidemiological factors, including for example, socio-demographic factors, density of the population, natural disasters, hygiene levels and so on. Areas with greater poverty may be particularly susceptible to the rapid spread of infection and thus the deleterious effects of resistance. In a similar way to that discussed above in relation to individuals, whole countries may choose to ‘free ride’ on the containment policies operated in other settings, suggesting that the total effort devoted to containing antimicrobial resistance is likely to be sub-optimal because some nations will rely on the efforts of other nations (Smith & Coast, 2002).

Despite the importance of the global issue in this context, economic assessments from all normative perspectives tend to be conducted on a national basis as if systems are closed to the outside world.

# **ECONOMIC RESPONSES TO THE CHALLENGE OF ANTIMICROBIAL RESISTANCE AND THEIR CONSIDERATION OF DISTRIBUTIONAL EFFECTS**

It is clear that there are many distributional issues facing economists working in the area of antimicrobial resistance, and also that these may be dealt with differently within the different normative approaches to economic analysis. The paper now turns to the questions that have been considered by economists and examines both their normative starting point and whether, and if so how, they have taken account of distributional effects within their analyses. The paper does not in any sense attempt to cover the entire literature related to the economics of antimicrobial resistance, instead it selects particular empirical examples that act as exemplars of the types of study available, illustrating the importance of both the normative viewpoint and the particular distributional issues discussed above in arriving at an overall interpretation of the economic analysis. Further, from the four types of economic contribution outlined at the start of the paper, it works with just two: assessing the costs of resistance, and evaluating policy options for containing resistance. The first of these is more closely related to positive economics (aiming to explain and predict) whilst the second is clearly located in the arena of normative analysis. The first area is examined, however, because it frequently provides a starting point for, and information used in, the second area.

## **Assessing the costs of resistance**

Assessments of the cost of resistance are often very narrow, focusing just on the current population, and very often on only health service (and often only hospital) costs. There are a number of such examples (see, among many others (Carmeli et al., 1999; Cosgrove, 2006; Parvizi et al., 2010; Alam et al., 2009)), but one of the most commonly cited is that by Cosgrove and colleagues (Cosgrove et al., 2002). This paper compares those with a resistant infection to matched controls with no such infection and examines mortality, hospital stay and hospital charges, concluding that, after adjusting for

confounding, resistance resulted in a median increase in hospital stay of 9 days and an increase in hospital charges of almost \$30,000. Although a nicely executed paper, this work also shows many of the limitations of current assessments of the cost of resistance. There is no attempt to go beyond the very narrow setting either in relation to time or geography, and the focus is very much on costs to the health system, suggesting a link to the narrower extra-welfarist health gain paradigm.

A broader assessment of cost linked more closely to a welfarist approach has attempted to look at costs to the whole economy. This work produces estimates of costs related to the impact of resistance on the labour market and the subsequent economic implications in terms of impacts on employment and inflation using general equilibrium analysis (Smith et al., 2005). Within such models people feature largely as labour inputs to the economy and consumers of its outputs. Although providing a broader assessment of costs, such work has until recently tended to focus on the current time period and a single country setting, although a similar approach has recently been applied as work for the UK O'Neill review which has considered costs globally and into the future (Taylor et al., 2014).

This suggests that in current cost assessments we may not be sufficiently accounting for the claims of some of those who should be taken into account. One aspect of cost that has largely been ignored, but which has recently been highlighted is the potential future loss within many other areas of the health system that might be incurred by an inability to provide treatments that rely on good infection control. This work, although largely speculative, has started to highlight costs that might be incurred by future generations if resistances emerge for which there are no treatments, considering aspects such as the potential inability to provide elective surgery and treatments that require immunosuppression (Smith & Coast, 2013). Such work is likely to be vital in highlighting the intergenerational nature of antimicrobial resistance and the current focus only on the current generation. Yet, even this could go further, in going beyond the health system, and in going beyond national boundaries. It could also consider costs not just in terms of lost health but also lost opportunities for people to live lives they have reason to value, that is, loss in capability wellbeing.

## **Evaluating policy options for containing resistance**

The empirical evaluation of policy options for containing resistance is the area where the normative approaches to economic analysis are most clearly focused. A recent paper focusing on the possibility of using subsidies for new combination antimalarial drugs provides a good example of an analysis conducted very much in the welfarist vein (Laxminarayan et al., 2010). The paper describes its focus as being on ‘economic efficiency’ and it does not consider distributional effects. This paper examines subsidies for artemisinin combination treatments (more expensive but more likely to protect from the development of resistance) in malaria-endemic countries over a twenty year period and explores the justification for this option compared to no subsidy in terms of efficiency from a welfarist perspective. It generates a complex model and concludes that such subsidies are indeed economically efficient in the vast majority of the scenarios that it examines. It does not consider what type of person is most likely to benefit from the subsidy nor does it consider impact on future generations or whether there are likely to be impacts on other settings. It uses a 3% discount rate<sup>5</sup> to deal with time-preference issues, and it uses \$50,000 for the value of a life lost, with this latter value being based on external work (Miller, 2000). Although not stated within the paper, within the welfarist approach, the role of the economist is seen as being appropriately limited to consideration of these economic issues and it would be for policy makers to consider the subsequent distributional issues. Distributional issues that a policy maker might wish to focus on might be around the particular groups who make use of the subsidy, although they may also be interested in the narrow policy options considered and whether other options around socio-economic development might offer more promise. (Tusting, Willey, Lucas, Thompson, Kafy, Smith et al. 2013)

A second paper also illustrates the welfarist perspective, but in this case using a general equilibrium model to explore the macroeconomic implications of policies to contain MRSA (Smith et al., 2006). The policies explored are the use of regulation, taxation and tradeable permits, and extensive assumptions about the level at which each policy might operate, its likely costs and its likely impacts were required. The paper tentatively concluded that permits would offer the most efficient solution

but much of the focus of the paper was on the feasibility of the method and the difference between analysis from a healthcare and a whole economy perspective. In itself, the paper does not consider distributional issues, but it does draw on earlier work by the same authors which explored each of these options in some depth, thinking not just about their economic but also their distributional impact and their likely feasibility (Coast et al., 1998). This earlier paper focused on a UK setting and noted particularly the likely distributional effects for current patients of any policy to impose additional charges/taxes on antibiotics. Such charges would be likely to be inelastic, that is, demand would be likely to remain relatively high following imposition of the charges, suggesting that charges might have to be quite high before making much impact. Such charges would also be regressive, and thus would be likely to impact most on those with low incomes. And finally, in an area where people might not have good information about their own health, imposing such charges could result in people failing to seek care in a timely manner or not complying with the advice of the health professional thus potentially resulting in those with severe problems suffering disproportionately as a result of the charge.

A third paper illustrates the extra-welfarist perspective, exploring the cost-effectiveness of a diagnostic test to inform antibiotic prescribing decisions, with the aim being to determine its impact on whether an antibiotic is prescribed as well as its impact on health, assessed using QALYs (Oppong et al., 2013). The paper focuses only on current prescribing decisions and does not attempt to take account of resistance developing as a result of these decisions. The concern of the paper is, however, to reduce free-riding amongst those who do not have a clinical need for antibiotic treatment (but who may still perceive the antibiotic as beneficial). Additionally, the outcome concerned with prescription of antibiotics could be seen as a proxy for impact on future generations. Again, the paper does not discuss distributional issues but draws its interpretations around cost-effectiveness from the cost per QALY gained associated with the diagnostic testing.

Given the early stage of application of the capability approach within economic analysis, as yet, there are no economic studies that the authors are aware of that have used a capability approach in assessing policy or interventions related to antimicrobial resistance, but work from this normative perspective should perhaps be encouraged given interest in the approach (Millar, 2013).

## **DISCUSSION: ECONOMICS, ETHICS AND ANTIMICROBIAL RESISTANCE**

The paper has set out three alternative normative approaches to economic assessment, described as the welfarist, extra-welfarist (health gain) and the capability approaches, and has attempted to consider how they might impact upon economic assessments within the area of antimicrobial resistance. It has attempted to do this in two ways. First, the paper examined some distributional challenges inherent to the challenge of antimicrobial resistance, focusing on the free-rider problem and distribution amongst individuals, the time preference problem and distribution amongst generations and the global nature of the problem and inter-regional distribution. It was suggested that the different normative approaches would have different implications for how these issues might be dealt with in economic evaluations. Second, the paper turned to consider the empirical work done by economists in this area. Although such empirical applications are relatively limited they are increasing in number and the paper considered examples of work done within two of the paradigms, both in relation to estimating the costs of resistance (a largely positive question, but one that draws on normative frameworks) and to economic assessments of policies and interventions. Unsurprisingly, given its relatively new and innovative nature, no economic assessments conducted using a capability approach were identified. Distributional effects were not considered explicitly within the empirical examples although for one paper they were considered in an associated paper.

The paper has both strengths and weaknesses. In terms of strengths, first, it considers distributional issues in the context of economic analysis of antimicrobial resistance from three normative approaches to economic analysis, clearly delineating between them. Second, it considers these approaches both in relation to theoretical issues intrinsic to evaluation of antimicrobial resistance policy, and to empirical studies that have been conducted. A weakness is that the paper does not present a comprehensive examination of all empirical studies undertaken but instead focuses on illustrative examples; nevertheless it highlights the focus on efficiency at the expense of consideration of distributional consequences.

A clear implication of this work for the practice of economic evaluation is that there should be enhanced exploration of distributional issues both in the choice and variation of values included within the analysis (such as discount rates) and in the subsequent interpretation of findings. In relation to interpretation, this might include both statements around the particular distributional assumptions contained within the methodology used, and the implications of the particular analysis in distributional terms. Where distributional issues are uncertain this should be highlighted.

There are a number of areas that would be worthy of future research. First, there are aspects of the particular approaches to economic evaluation that could benefit from further exploration if they are to be incorporated in future economic assessments. These include both option value within the welfarist approach, and agency within the capability approach. Assessing the extent to which economic evaluations are able to handle issues of agency and the implications of this for evaluations of resistance would be particularly valuable. Second, also in relation to the capability approach, empirical application of the method in the context of antimicrobial resistance would be helpful so that its distributional implications in practice can be clarified. Third, methods for assessing distributional impact could be applied alongside assessments of economic efficiency in empirical evaluations of resistance so as to better clarify the important distributional considerations for future work.

To conclude, a key message from this paper is that all economic analysis is not the same; there are different approaches aligned with different philosophical bases. These different starting points may fundamentally affect how distributional issues are handled although current empirical evidence is limited, particularly for assessments conducted from a capability perspective. Economists could, and should, give greater attention to distributional implications in reporting and interpreting economic evaluations of interventions and policies for containing antimicrobial resistance.

## NOTES

1. It should be noted that there are, however, concerns about this approach among some economists (Harsanyi, 1955).
2. Although note that there may also be positive externalities associated with reduced transmission of infection to others (Coast et al., 1998).
3. Although superficially similar, this differs from option value within the welfarist approach, which is concerned with personal utility from retaining the possibility of using a good or service in the future, as opposed to the sense of moral responsibility associated with agency.
4. Although there are two reasons why this might not be the case. The first concerns the ‘fitness cost’ for micro-organisms of retaining resistance, which means that for some antimicrobials, reduction in use may result in a loss of resistance (Magee, Pritchard, Fitzgerald, Dunstan, Howard & Welsh Antibiotic Study Group, 1999; Spratt, 1996). The second concerns the possibility of developing new antimicrobials to replace those to which resistance has developed (Norrby, Nord, Finch & ESCMID, 2005). There is substantial uncertainty around both of these issues.
5. This means that \$100 of benefit gained in the last year of the study would be worth around \$55 in terms of its present value.



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